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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,288	08/20/2003	Paul Diamond	PT100-3	5798

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
10/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,288	DIAMOND, PAUL	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-16,21,23,26,28,31 and 33-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-20,22,24,25,27,29,30,32 and 36-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office action.

2. Claims 1-16, 21, 23, 26, 28, 31, and 33-35 have been withdrawn. Claim 18 has been amended. Claims 39 and 40 are new.

Claims 17-20, 22, 24, 25, 27, 29, 30, 32, and 36-40 are under examination.

Response to Arguments

Claim Rejections - 35 USC § 112, enablement

3. The rejection of claims 17-20, 22, 24, 25, 27, 29, 30, 32, and 36-38 under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement, is withdrawn in response to Applicant's arguments filed on 07/15/2007.

Claim Rejections - 35 USC § 101

4. Claims 18, 19, 22, 24, 29, 30, and 32 remain rejected under 35 U.S.C. 101, as being directed to non-statutory subject matter. Applicant's arguments filed 07/15/2007 have been fully considered but they are not persuasive.

Applicant submits that, as discussed during the interview of 065/2007, an explicit disclaimer of the scope of the claims encompassing a human being should be responsive to the instant rejection without raising any new matter issues.

Applicant's argument is acknowledged, however, the rejection is maintained because Applicant's disclaimer is not enough to overcome the rejection, since the claims encompass a cell that is part of a human being.

Amending the claims to recite an isolated cell would obviate this rejection.

New Rejections

Claim Rejections - 35 USC § 112, enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 18-20, 22, 24, 29, 30, 32, 36, and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a cell wherein a pre-selected DNA sequence is excisable from the cellular genome in response to the presence in the cell of a nucleic acid complementary to the mRNA encoding the repressor protein, does not reasonably provide enablement for a cell wherein a pre-selected DNA sequence is excisable from the cellular genome in response to the presence in the cell of a nucleic acid having at least one region of pre-determined sequence such that the expression of site specific recombinase is derepressed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure meets the

enablement requirement of 35 USC § 112, first paragraph, have been described by the court in *In re Wands,* 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skills of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided.

The instant claims are drawn to a cell comprising (i) an excisable sequence flanked by specific excision sequences, (ii) a repressible promoter linked to a gene encoding recombinase specific for the excision sequences, and (iii) a gene encoding a repressor protein specific for the repressible promoter; excision takes by RNA silencing cause by the presence in the cell of a RNA with predetermined sequences. Applicant contemplates to use silencing to inhibit repressor protein expression, which in turn derepresses the promoter leading to the recombinase expression and excision of the pre-selected sequence from the genome. Therefore, obtaining such a cell requires a specific complementary RNA, i.e., a RNA complementary to the mRNA encoding the repressor protein. However, the claims are much broader than this, since they encompass any RNA with any predetermined sequences, wherein the RNA could be complementary to practically any transcript in the cells and could silence any transcript

in the cell. The art teaches that gene silencing is very specific and that the silencing RNA must be complementary over its entire length to the targeted gene. One of skill in the art would not recognize that just any RNA having at least one region predetermined sequence, as generally claimed, can work as claimed.

In conclusion, the claims are only enabled for cell wherein a pre-selected DNA sequence is excisable from the cellular genome in response to the presence in the cell of a nucleic acid complementary to the mRNA encoding the repressor protein

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 17-20, 22, 24, 25, 27, 29, 30, 32, and 36-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oliver et al. (U.S. Patent No. 5,723,765, incorporated by reference in the instant specification), in view of Porter (Trends Genet, 1998, 14: 73-79).

Oliver et al. teach a method of making a genetically modified plant by regenerating a whole plant from a genetically plant cell, wherein the genetically modified plant cell comprises (i) DNA sequences having a pre-selected gene linked to a pre-selected constitutively active promoter, wherein the gene and the promoter are separated by a blocking sequence flanked on each side by specific excision sequences,

(ii) a gene encoding a recombinase that recognizes the specific excision sequences linked to a repressible promoter, and (iii) a gene encoding the repressor protein specific for the repressible promoter; the expression of the repressor protein is controlled by an outside stimulus, wherein the application of the stimulus blocks the repression of the recombinase leading to the excision of the excisable blocking sequence (claims 17, 18, 20, 37, and 38) and brings the pre-selected gene under the control of the pre-selected promoter (claims 25, 27, 29, 32, 36, 39, and 40) (Abstract, column 1, lines 58-67, column 3, lines 1-67, column 4,lines 40-65, column 7, lines 7-20). Oliver et al. also teach that the blocking sequence may contain an herbicide resistance gene, i.e., the excisable element comprises an expression cassette with a pre-selected gene (claims 19 and 30) (column 5, lines 30-32). Oliver et al. do not teach causing RNA silencing against the mRNA encoding the repressor (claims 17, 18, 22, 24, 25, and 29). However, this is not innovative over the prior art, which teaches silencing of pre-selected genes by introducing into cells a nucleic acid complementary to all or part of the pre-selected genes, wherein the complementary nucleic acid could be a RNA (see for example Porter, p. 78, columns 1 and 2). Because Oliver et al. and Porter teach methods of inactivating pre-selected genes, it would have been obvious to one of skill in the art, at the time the invention was made, to substitute one method for the other to achieve the predictable result of inactivating the desired gene.

9. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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